

Serum-prolactin levels in patients with vitiligo

Serum-prolactin and vitiligo

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Aim: This study aims to determine the relationship between prolactin, an important in vivo modulator of cellular and humoral immunity, and vitiligo in whose etiopathogenesis autoimmunity is thought to play a role. **Material and Method:** A total of 36 patients, 20 females and 16 males, clinically and histopathologically diagnosed with vitiligo, and total 40 healthy individuals, 26 females and 14 males, who are compatible in age and sex, were included in this study. The average age of the patients is 28.3 ± 13.9 ranging from 8 to 56, and the average age of the control group is 27.6 ± 13.8 ranging from 7 to 55. Prolactin levels were measured in both groups. The descriptive statistics of the collected data were calculated. **Results:** Fifty-six percent of the patients were women, and 44% were men; and 65% of the control group were women and 35% were men. The serum prolactin levels of the patients ranged from 3.58 to 59.45 with the mean of 7.98 ± 4.45 , and the serum prolactin levels of the control group ranged from 4.81 to 22.37 with the mean of 7.53 ± 3.61 , and there was no statistically significant difference between the two groups ($p > 0.05$). **Discussion:** Although the incidence of various autoantibodies and autoimmune diseases in patients diagnosed with hyperprolactinemia was found to increase, there were no statistically significant results of prolactin in the etiopathogenesis of vitiligo due to the limited number of patients in this study. There is a need for further studies with more patient and at receptor-level in order to obtain definite results.

Keywords

Vitiligo; Prolactin; Autoimmune Diseases

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Introduction

Vitiligo is a disease caused by loss of melanocytes in the skin and characterized by sharply-circumscribed depigmented macules, and its cause is unknown [1]. It is a commonly seen public disease and leads to important cosmetic problems. Many hypotheses have been suggested on the etiopathogenesis of vitiligo, but the cause has not yet been fully revealed. Among the most discussed ones are neural autoimmune and autocyotoxic hypotheses [2].

The incidence of various autoantibodies and autoimmune diseases has been found to increase in hyperprolactinemia-detected patients. However, many studies have shown that prolactin (PRL) has stimulatory and regulatory functions in the immune system. A relationship has also been revealed between PRL levels and many autoimmune diseases such as Psoriasis, Behçet's disease, SLE, RA, Sjögren's syndrome, dermatomyositis [3].

In this study, we investigated whether PRL, an important modulator of cellular and humoral immunity, is associated with vitiligo, in whose etiopathogenesis autoimmunity is thought to play a role. In this direction, serum PRL levels were compared between vitiligo patients and healthy control group.

Material and Method

A total of 36 patients, 20 females and 16 males, who were admitted to our clinic and who were clinically and histopathologically diagnosed with vitiligo and a total of 40 healthy individuals as a control group, 26 females and 14 males, who are suitable in terms of age and sex distribution were included in the study. Control group consisted of healthy volunteers.

Patients were questioned in detail regarding age, gender, clinical types of vitiligo, the age of onset, duration of the disease, history of vitiligo in the family, as well as the presence of other autoimmune systemic and skin diseases (such as thyroid diseases, SLE, RA, diabetes mellitus).

Those with menstrual irregularity, chronic renal failure and chronic liver disease that may cause changes in serum PRL levels, those who use the medication modifying the PRL levels (oral contraceptives, thyroid hormone preparations, phenothiazines, opiates, L-dopa, apomorphine, bromocriptine and related ergot derivatives), those with extreme stress, pregnancies, women in lactation period, those who received cranial radiotherapy and pituitary adenomas surgery, and those with amenorrhea, galactorrhea, gynecomastia, hirsutism, decreased libido, impotence and known prolactinomas were not included in the patient and control groups.

Patients and control subjects were informed that the blood sample should be given on an empty stomach after an uninterrupted night's sleep and should avoid nipple warnings before giving examples so that serum PRL levels would not be affected. Serum PRL levels were measured using Roche® Prolactin II kit with electro-chemiluminescence immunoassay method at the Department of Biochemistry of Dışkapı Yıldırım Beyazıt Training and Research Hospital. Normal values were 4.79 - 23.3 ng/ml for women and 4.04 - 15.2 ng/ml for men.

Statistical Analysis

Analysis of the data was conducted in SPSS for Windows 11.5 package program. Whether the distribution of continuous variables is close to normal was investigated by the Shapiro Wilk

test. Descriptive statistics were shown as mean \pm standard deviation or median (minimum- maximum) for continuous variables, and categorical variables as number of cases and percentage (%). The significance of the between-group difference in terms of averages was examined by the Student's t-test and the significance in terms of the median values by the Mann-Whitney U test. Categorical variables were assessed by Pearson's Chi-Square or Fisher's Exact Chi-Square test. For $p < 0.05$, the results were considered statistically significant.

Results

Age:

The ages of the patients ranged from 8 to 56 and the mean age was 28.3 ± 13.9 , and the age of the controls ranged from 7 to 55 and the mean age was 27.6 ± 13.8 years. The average age of the female patients was 31.15 ± 14.58 , and the average age of the controls was 30.26 ± 13.98 . Mean age of the male patients was 25.43 ± 13.32 , and mean age of the controls was 25 ± 13.61 . There was no statistically significant difference between these values ($p > 0.5$).

Gender:

Fifty-six percent of the patients were women, and 44% were men; 65% of the controls were women and 35% were men. No statistically significant difference was found between the two groups in terms of gender distribution ($p > 0.05$).

The types of Vitiligo:

Generalized vitiligo was found in 20 patients (55.6%), focal type in 11 patients (30.6%) and acrofacial type in 5 patients (13.9%). For male patients, 8 have generalized type (50%), 5 have focal type (31.3%) and 3 have acrofacial (18.7%) while, for female patients, 12 have generalized type (60%), 6 have focal type (30%) and 2 have acrofacial type (10%).

The average age of onset:

The average onset age of vitiligo patients was 26.25 ± 12.81 , the age of onset in female patients ranged from 8 to 50 years with the average onset age as 28 ± 12.51 , and the age of onset in male patients varied from 7 to 53 years with the average onset age as 24.06 ± 13 .

Serum prolactin level:

Serum prolactin levels of the patients range from 3.58 to 59.45 and the mean level is 7.98 ± 4.45 and serum prolactin levels of the controls range from 4.81 to 22.37, with a mean of 7.53 ± 3.61 , and there was no statistically significant difference between the two groups ($p > 0.05$). Mean serum prolactin levels of the women in the patient group were 9.22 ± 5.6 and mean serum prolactin levels in the control group were 7.92 ± 3.82 , and no statistically significant difference was found between them ($p > 0.05$).

Serum prolactin level by gender:

The mean serum prolactin levels of the males in the patient group were 6.75 ± 3.8 and the mean serum prolactin levels of those in the control group were 7.15 ± 3.39 , and there was no statistically significant difference between them ($p > 0.05$).

The average prolactin level by vitiligo type:

Male and female vitiligo patients were compared in terms of vitiligo type. The average prolactin level of patients with generalized vitiligo was calculated as 7.46 ± 4.56 , those with focal vitiligo 6.39 ± 2.88 and those with acrofacial vitiligo as 7.52 ± 2.46 , and no statistically significant difference was found between vitiligo type and average prolactin levels ($p > 0.05$). The average prolactin level of female patients with generalized vitiligo was 13.29 ± 5.82 , the average of focal vitiligo patients was 7.91 ± 3.11 , and the average of acrofacial vitiligo patients was 6.26 ± 0.71 . There was no statistically significant difference between the type of vitiligo and the average prolactin levels ($p > 0.05$).

Mean prolactin level by the presence of autoimmune disease:

Seven of the female vitiligo patients (19.44%) and four of the male vitiligo patients (11.11%) had an autoimmune disease.

The mean prolactin level in female patients was 12.80 ± 5.42 and the difference was not statistically significant compared to the mean prolactin level of female vitiligo patients without autoimmune disease ($p > 0.05$).

The mean prolactin level in male patients was 6.46 ± 2.33 and no statistically significant difference was found when compared to the mean prolactin level of male vitiligo patients without autoimmune disease ($p > 0.05$).

Mean prolactin level by age of onset:

The mean age of onset of vitiligo patients was calculated as 26.25 ± 12.81 . There was no statistically significant difference between the age of onset and mean prolactin level ($p > 0.05$).

Discussion

In this study, we demonstrated that there were no statistically significant results of prolactin in the etiopathogenesis of vitiligo patients.

Vitiligo is a depigmentation disease which cause is unknown and characterized by sharply-circumscribed white macules, resulting from loss of melanocytes in the skin. Although it is thought that this disease is seen in the rates of 0.14 - 8.8% without discrimination of age, sex, and race, its possible incidence is 1 - 2% [4].

Both genders are equally affected by the disease, but in some studies, the dominance of female patients is due to the fact that women are more sensitive to cosmetic disorders and want to start treatment earlier [3,5]. Of the 36 patients in this study, 20 were female (55.5%) and 16 were male patients (44.5%). Although there was no statistically significant difference, female predominance was determined in patients who applied to our clinic and included in the study.

In patients with generalized vitiligo from which a large number of family members have been affected, the age of onset was found to be earlier than vitiligo patients who have no family history. Families with vitiligo have an early age of onset [6]. The disease may break out at any time between birth and the age of 81. In 50% of cases, the disease starts between the ages of 10 and 30 [4]. The ages of the patients in this study were between 8 and 56 years, and the mean age of the patients was 28.3. The onset age of their disease was between the earliest

7 years of age and the latest 53 years of age, and the average age of onset was calculated as 26.25. The mean duration of illness was 12 months.

It has been found out that one family member in more than 30% of vitiligo patients is likely to be affected and the first generation family members in more than 21% of them are likely to be affected [7].

Studies have shown that vitiligo is associated with autoimmune diseases, these diseases are increasingly detected in first-degree relatives of patients, and that there are a great variety of vitiligo-associated autoimmune diseases [6]. In our study, the cases with coexisting autoimmune diseases such as thyroid disease, pernicious anemia, SLE, diabetes, RA, and alopecia areata account for 30.5% of vitiligo patients.

Patients included in the study are divided into the types of focal, generalized and acrofacial. Of all the patients, 20 had a generalized type (55.6%), 11 focal type (30.6%) and 5 acrofacial type (13.9%). Of female patients, 12 were generalized (60%), 6 were focal (30%) and 2 were an acrofacial type (10%). Of male patients, 8 were generalized (50%), 5 were focal (31,3%) and 3 were acrofacial (18,7%). Like in other studies, the most common vitiligo type in our study was the generalized type, followed by focal and acrofacial types.

Studies on the pathogenesis of vitiligo include multifactorial and polygenic evidence [8]. Vitiligo is an inherited feature with incomplete transition, multiple locus, non-Mendelian pattern characterized with genetic heterogeneity [8]. For its etiopathogenesis, various theories have been proposed that explain the loss of epidermal melanocytes. These are examined under the title of neural theory, autoimmune theory, autocytoxic theory [1]. Vitiligo and autoimmunity relationship has been shown to increase both with autoantibodies and with the frequency of accompanying autoimmune diseases, and it has also been reported that PRL serum levels have increased in a number of autoimmune diseases such as rheumatoid arthritis (RA), multiple sclerosis, primary Sjögren syndrome, systemic sclerosis (SSc), psoriasis and uveitis and in particular to SLE, and this increase is thought to play a role in the pathogenesis of diseases [3,9]. Today, PRL, also considered a T cell cytokine, is produced by many tissues and cells, including skin cells and immunocytes, except for the anterior pituitary [4]. PRL receptor [10], a member of the cytokine/hematopoietic receptor superfamily with the pituitary origin, is found on many immune system cells such as lymphocytes, monocytes, neutrophils, NK cells and thymic epithelial cells [11]. PRL activates protein kinase C, which is required for T cell proliferation and increases IFN γ production through IL-2 receptor expression and interferon regulatory factor 1 (IRF-1). IRF-1 is important for differentiation of T and B cells. Thus, PRL stimulates both antibody production and increases total T and CD2+lymphocyte ratio [11].

Kaçar et al. [12] have investigated PRL levels in RA and SLE patients, and they reported that the PRL is high in patients with RA and at the same time is in parallel with the activity of the disease; however, they stated that they did not find a relationship between SLE and PRL in the same direction. Hyperprolactinemia was detected in male and female patients with systemic sclerosis, and the lymphocytes of these patients have been shown both to produce increased amounts of PRL and to

carry PRL receptors. In the same study, it was determined that the production of soluble IL-2 receptor (CD25), an immunological indicator of systemic sclerosis disease activity from lymphocytes with the effect of PRL, was increased, and it was suggested that PRL may be responsible for immunological changes in systemic sclerosis [9].

In animals that were accepted as a model for MS and in which allergic encephalomyelitis was experimentally produced, PRL levels were found to be high at the onset of the disease and bromocriptine suppressed the attacks [13]. In various studies conducted on patients with Sjögren's syndrome, PRL levels were found to be 1.3 to 2.4 times greater than controls [14]. Kavala et al. [15] found that serum PRL levels in male patients with pemphigus were not significantly higher than those in the control group, but significantly higher in female patients. In the activation period, serum PRL levels in both genders were significantly higher than the control group. There was no significant difference in the serum PRL levels between the male and female patients in remission and the control group. Giasuddin et al. [16] measured serum PRL levels in 12 patients with psoriasis and compared them with the control group, considering the presence of PRL gene and HLA complex on chromosome 6 and the hyperproliferative effect of PRL in patients with psoriasis vulgaris. In three patients, they found an increased level of prolactinoma and reported this is statistically significant.

We have also compared the serum PRL levels of the vitiligo patients and control group, aiming to determine the relationship between vitiligo in which etiopathogenesis autoimmunity is thought to play a role and PRL which is an important modulator of cellular and humoral immunity. Although there were three hyperprolactinemic cases in the patient group, there was no statistically significant difference in serum PRL levels between the two groups.

When we looked at serum PRL levels according to vitiligo type, there was no statistically significant difference between genders even though there were higher values in female patients, especially those with generalized type. No significant difference was found between the presence of additional autoimmune disease, the onset of disease and serum PRL levels.

Although there have been many studies investigating PRL levels in various autoimmune diseases, only one study conducted to detect PRL levels in vitiligo patients has been encountered in the literature. Similarly, Gönül et al. [17] did not find a significant difference in terms of age, sex, duration of illness and family history with PRL levels between vitiligo patients and control group.

Limitations

This is an observational and single-institution study that has a relatively small sample size. Thus, it is subject to various unaccountable confusing factors natural to such an analysis. Additionally, we could not compare other markers, because they were not routinely measured in our study population.

Conclusions

Our study does not support the presence of a direct relationship between PRL, which is known to increased serum levels in autoimmune diseases, and vitiligo, in whose etiopathogenesis

autoimmunity is thought to play a role. No significant difference was found between serum PRL levels between 36 patients and 40 controls. Also, there was no significant difference between serum PRL levels and duration of disease, the age of onset, the presence of additional autoimmune disease, and the type of vitiligo. In order to obtain healthier results, we assume that we can make a healthier interpretation with the larger patient group and by continuing the investigation of PRL receptors in the cells and their responses to PRL although serum PRL levels are normal.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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